In the Claims

Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1. (Previously Presented) A non-naturally occurring protein which inhibits human neutrophil elastase and which is a protein comprising at least the core sequence of a non-naturally occurring Kunitz domain, said Kunitz domain being more similar in sequence to the core sequence 26-76 of ITI-D1 than to the core sequence 5-55 of BPTI, when its cysteines are aligned with those of BPTI and ITI-D1, but said domain differing from ITI-D1 in that at least one of the following conditions applies:
(a) the residue corresponding to BPTI residue 15 and ITI-Dl residue M36 is Val or Ile,
(b) the residue corresponding to BPTI residue 16 and ITI-Dl residue G37 is Ala,
(c) the residue corresponding to BPTI residue 18 and ITI-Dl residue T39 is Phe,
(d) the residue corresponding to BPTI residue 19 and ITI-D1 residue S40 is Pro,
(e) the residue corresponding to BPTI residue 1 and ITI-D1 residue K22, if any, is Arg,
(f) the residue corresponding to BPTI residue 2 and ITI-D1 residue E23, if any, is Pro, or
(g) the residue corresponding to BPTI residue 4 and ITI-D1 residue S25, if any, is Phe.

2. (Previously Presented) The protein of claim 1 which differs from human ITI-D1 at least one of the positions corresponding to BPTI positions 15-20.

3. (Previously Presented) The protein of claim 1 where, in said Kunitz domain, BPTI positions 1-4 are Arg-Pro-Asp-Phe (residues 1-4 of SEQ ID NO:17).

4. (Currently Amended) The protein of claim 1 where, in ~~the~~ said Kunitz domain, the residue corresponding to BPTI position 31 is Glu.

5. (Currently Amended) The protein of claim 1 where, in ~~the~~ said Kunitz domain, the residue corresponding to BPTI position 31 is Gln.

6. (Currently Amended) The protein of claim 1 where, in ~~the~~ said Kunitz domain, the residue corresponding to BPTI position 34 is Val.

7. (Currently Amended) The protein of claim 1 where, in said Kunitz domain, the residue corresponding to BPTI position 4 is Phe.

8. (Currently Amended) The protein of claim 1 where, in said Kunitz domain, the residue corresponding to BPTI position 2 is Pro.

9. (Currently Amended) The protein of claim 1 where, in ~~the~~ said Kunitz domain, the residue corresponding to BPTI position 1 is Arg.

10. (Currently Amended) The protein of claim 1 where, in ~~the~~ said Kunitz domain, the residue corresponding to BPTI position 26 is Ala.

11. (Currently Amended) The protein of claim 1 where, in ~~the~~ said Kunitz domain, the residue corresponding to BPTI position 18 is Phe.

12. (Currently Amended) The protein of claim 1 where, in said Kunitz domain, the residue corresponding to BPTI position 15 is Val or Ile, 16 is Ala or Gly, 17 is Met or Phe and 19 is Pro or Ser.

13. (Previously Presented) The protein of claim 1 which has an affinity for HNE such that its KD is less than 10^{-8} M.

14. (Previously Presented) The protein of claim 1 which has an affinity for HNE such that its KD is less than 10^{-9} M.

15. (Previously Presented) The protein of claim 1 which has an affinity for HNE such that its KD is less than 10^{-11} M.

16. (Previously Presented) The protein of claim 1 wherein both conditions (a) and (c) apply.

17. (Previously Presented) The protein of claim 16 wherein condition (d) also applies.

18. (Previously Presented) The protein of claim 1 wherein conditions (e) -.(g) apply.

19. (Previously Presented) The protein of claim 16 wherein conditions (e) - (g) also apply.

20. (Previously Presented) The protein of claim 17 wherein conditions (e) - (g) also apply.

21. (Previously Presented) The protein of claim 1 where said Kunitz domain is a reference domain selected from the group consisting of BITI-E7-1222, AMINO1 (SEQ ID NO:22), AMIN02 (SEQ ID NO:23), MUTP1 (SEQ ID NO:24), BITI-E7-141 (SEQ ID NO:17), MUTT26A (SEQ ID NO:18), MUTQE (SEQ ID NO:19), and MUT1619 (SEQ ID NO:20) or a Kunitz domain comprising an amino acid sequence which otherwise differs from the core sequence of one or more of said reference domains solely by one or more class A and/or one or more class B substitutions as set forth in Table 65.

22. (Previously Presented) The protein of claim 1 where said non-naturally occurring Kunitz domain is a reference domain selected from the group consisting of BITI-E7-1222, AMINO1, AMIN02, MUTP1, BITI-E7-141, MUTT26A, MUTQE, and MUT1619 in Table 220 or a kunitz domain comprising an amino acid sequence which differs from the core sequence of one or more of said reference domains solely by one or more class A substitutions as set forth in Table 65.

23. (Previously Presented) The protein of claim 1 where the core sequence of said Kunitz domain consists of an amino acid sequence identical to that of the core sequence of a reference domain selected from the group consisting of BITI-E7-1222, AMIN01, AMIN02, MUTP1, BITI-E7-141, MUTT26A, MUTQE, and MUT1619 in Table 220.

24. (Previously Presented) The protein of claim 1 where said Kunitz domain is selected from the group consisting of BITI-E7-1222, AMIN01, AMIN02, MUTP1, BITI-E7-141, MUTT26A, MUTQE, and MUT1619 in Table 220.

25. (Previously Presented) The protein of claim 24 where said protein further comprises at least a functional portion of a coat protein of a filamentous phage, sufficient to cause display of said protein on the surface of a filamentous phage particle if said protein is expressed, together with the other proteins of said phage, in a cell capable of assembling said particles.

26. (Previously Presented) The protein of claim 25 where said coat protein is the one corresponding in said filamentous phage to the gene III protein of M13 phage.

27. (Previously Presented) The protein of claim 1 which is identical to a protein selected from the group consisting of BITI-E7-1222, AMINO1, AMIN02, MUTP1, BITI-E7-141, MUTT26A, MUTQE, and MUT1619 in Table 220.

28. (Previously Presented) The protein of claim 1 where said protein is BITIE7-141.

29. (Previously Presented) The protein of claim 1 where said protein is MUTT26A (SEQ ID NO:18).

30. (Previously Presented) The protein of claim 1 where said protein is MUTQE (SEQ ID NO:19).

31. (Previously Presented) The protein of claim 1 where said protein is MUT1619 (SEQ ID NO:20).

32. (Cancelled) The protein of claim 1 where said Kunitz domain is no identical in amino acid sequence to any of the Kunitz domain amino acid sequences set forth in Table 13 of Serial No. 08/133,031.

33. (Previously Presented) A method of inhibiting human neutrophil elastase (HNE) which comprises contacting the HNE with an inhibitor effective amount of a protein of any one of claims 1, 12, and 14-23.

34. (Previously Presented) A method of inhibiting harmful human neutrophil elastase activity in a subject which comprises administering to the subject an inhibitorily effective amount of a protein of any one of claims 1, 12 and 14-23.

35. (Previously Presented) A method of treating emphysema in a subject which comprises administering to the subject a therapeutically effective amount of a protein of claim 1.

36. (Previously Presented) A method of treating cystic fibrosis in a subject which comprises administering to the subject a therapeutically effective amount of a protein of claim 1.

37. (New) A non-naturally occurring protein which inhibits human neutrophil elastase and which is a protein comprising at least the core sequence of a non-naturally occurring Kunitz domain, said Kunitz domain differing from the core sequence 5-55 of BPTI, when its cysteines are aligned with those of BPTI in that at least one of the following conditions applies:
(a) the residue corresponding to BPTI residue 15 is Ile,
(b) the residue corresponding to BPTI residue 17 is Phe,
(c) the residue corresponding to BPTI residue 18 is Phe,
(d) the residue corresponding to BPTI residue 19 is Pro,
(e) the residue corresponding to BPTI residue 39 is Met,
(f) the residue corresponding to BPTI residue 40 is Gly,
(g) the residue corresponding to BPTI residue 41 is Arg, or
(h) the residue corresponding to BPTI residue 42 is Gly.

38. (New) The protein of claim 37, wherein conditions (a) through (h) apply.

39. (New) The protein of claim 38, wherein the core sequence is EpiHNE1.

40. (New) The protein of claim 37, wherein the core sequence is EpiHNE2.

41. (New) The protein of claim 37 which has an affinity for HNE such that its K_D is less than 2pM.

42. (New) The protein of claim 37 which has an affinity for HNE such that its K_D is less than 5pM.

43. (New) A non-naturally occurring protein which inhibits human neutrophil elastase and which is a protein comprising at least the core sequence of a non-naturally occurring Kunitz domain, said Kunitz domain being more similar in sequence to the core sequence 3-57 of ITI-D2 than to the core sequence 5-55 of BPTI, when its cysteines are aligned with those of BPTI and ITI-D2, but said domain differing from ITI-D2 in that at least one of the following conditions applies:
(a) the residue corresponding to ITI-D2 residue 3 is Glu,
(b) the residue corresponding to ITI-D2 residue 15 is Ile,
(c) the residue corresponding to ITI-D2 residue 18 is Phe,
(d) the residue corresponding to ITI-D2 residue 19 is Pro, or
(e) the residue corresponding to ITI-D2 residue 20 is Arg.

44. (New) The protein of claim 43, wherein conditions (b) through (d) apply.

45. (New) The protein of claim 43, wherein the core sequence is EpiHNE4.

46. (New) The protein of claim 43, wherein the core sequence is EpiHNE3.

47. (New) The protein of claim 43 which has an affinity for HNE such that its K_D is less than 5 pM.

48. (New) The protein of claim 43 which has an affinity for HNE such that its K_D is less than 7 pM.